

Remarks

I. General

In the Office Action dated October 8, 2003, the Examiner rejected pending claims 1-4 on three bases. The first is under 35 U.S.C. § 112, first paragraph; the second is under 35 U.S.C. § 102 for anticipation based on U.S. Patent No. 5,495,423 to DeLisi et al. (“DeLisi”); and the third is under 35 U.S.C. § 103 for obviousness base on DeLisi alone and DeLisi in view of U.S. Patent No. 6,251,620 to Hatada et al. (“Hatada”). Applicant will demonstrate that each of these bases for rejection is overcome and should be withdrawn, thereby placing the present application in condition for allowance.

Applicants would like to thank the Examiner for withdrawing the rejection associated with Applicants’ claim of priority.

II. The Claims are Enabled by the Specification

The Examiner rejected claims 1-4 under 35 U.S.C. § 112, first paragraph on the basis that they are enabled for de novo design of molecules that interact with receptor sites of Src-homology-3 domain, Src-homology-2 domain, MDM2 protein, CD4 protein, or human carbonic anhydrase II protein, but not for the de novo design of molecules that interact with any receptor. The receptor sites that have just been recited are the preferred receptor sites. (See, Specification page 60, lines 8-11). These examples of receptor sites are the best mode for carrying out the invention at the time the application was filed.

The best mode and enablement requirements are two separate and distinct requirements under 35 U.S.C. § 112, first paragraph. *Teleflex, Inc. v. Ficosa North America Corp.*, 299 F.3d 1313 (Fed. Cir. 2002). The best mode in the form of examples in the present application appear to be read by the Examiner as limitations to the scope of the claims and any receptor sites beyond them are not enabled. The case law, however, is clear that it is improper to limit the scope of claims to the preferred embodiment unless such a limitation is set forth in the specification or prosecution history. (See, *Northern Telecom Ltd. v. Samsung Electronics Co., Ltd.*, 215 F.3d 1281 (Fed. Cir. 2000); *TurboCare Division of Demag Delaval Turbomachinery Corp. v. General Electric Co.*, 264 F.3d 1111 (Fed. Cir. 2001)). Applicants have not so limited the claims and will have a scope that is supported by the specification beyond the preferred receptor sites.

The Specification at page 59, line 11 to page 60, line 8 describes the method of evaluating a receptor site for de novo design. Applicants describe at the bottom of page 22 and the top of page 23, that the crystalline structures of proteins and protein-ligands can be disassembled and the free energy contributions determined. This process is known and well within the capabilities of one skilled in the art without undue experimentation. Thus, the method of the present invention would result in the receptor sites that include but would not be limited to the preferred receptor sites Src-homology-3 domain, Src-homology-2 domain, MDM2 protein, CD4 protein, or human carbonic anhydrase II protein. Accordingly, the receptor sites that meet the criteria set forth by this method would be enabled by the disclosure of the present application beyond the preferred receptor sites. Thus, the pending claims are enabled by the specification beyond just the preferred receptor sites according to the disclosed method for evaluating the receptor sites to determine each's appropriateness for use. (See, *Mycogen Plant Science, Inc. v. Monsanto Co.*, 252 F.3d 1306 (Fed. Cir. 2001)). Accordingly, the enablement rejection has been traversed and should be withdrawn.

III. Claims 1-4 are not Anticipated

The Examiner has rejected claims 1, 3, and 4 under 35 U.S.C. §102 for anticipation based DeLisi. The Examiner contends that DeLisi teaches each and every element of the claims 1, 3, and 4 in the same way. Applicants submit that this error.

In the Applicants' previous amendment, the claims were amended to recite that the method uses "second generation molecules from one of more functional groups of the high-ranking molecules determined at Steps (a) and (b). The Examiner has contended that DeLisi discloses the use of second-generation molecules in its process. Applicants in the previous amendment stated that DeLisi does not teach or suggest the use of the second-generation molecules as set forth in the claims of the present invention.

The Examiner is hereby directed to Step (a) of claim 1 of the present application. At that step, the selection of fragments and their orientation is predicated on a free energy estimate that "may be higher than a lowest free energy estimate possible for the molecule." On the other hand, DeLisi builds molecules and selects fragments based on the minimum energy found and in no way contemplates the counterintuitive method of the present invention of using higher energy values in building first and second

generation molecules. Accordingly, DeLisi does not anticipate claim 1 of the present invention and this basis of rejection should be withdrawn.

Claims 3 and 4 depend from claims 1. Therefore, claims 3 and 4 add features to claim 1 and include claim 1's method of building molecules that use free energy estimates that may be higher than a lowest free energy estimate possible for the molecule. As such, these claims are not anticipated by DeLisi for the same reason claim 1 is not anticipated. Applicants, therefore, request that the anticipation rejection be withdrawn as it has been asserted against claims 3 and 4.

IV. Claims 1-4 are not Obvious

The Examiner has rejected claims 1, 3, and 4 under 35 U.S.C. §103 for obviousness based DeLisi. In view of *In re Gulack*, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983). The Examiner in applying *In re Gulack* to the DeLisi states that the case stands for defining that nonfunctional descriptive material will not distinguish the invention from prior art in terms of patentability. Although Applicants believe the Examiner was in error with regard to the conclusion reached regarding the distinguishing features of the "second generation molecule," Applicants want to point out, as was set forth in the previous section on anticipation, that claim 1 recites that the selection of fragments and their orientation is predicated on a free energy estimate that "may be higher than a lowest free energy estimate possible for the molecule." This is clearly not a "nonfunctional descriptive material" that distinguishes claim 1 from the Examiner's combination to form the rejection, but is clearly part of the defined claimed method for generating the first and second-generation molecules. Neither the combination of DeLisi and *In re Gulack* nor either of these references taken alone teach, suggest, or in any way render claim 1 obvious. Therefore, Applicants request the obviousness rejection be withdrawn as it has been applied to this claim.

Claims 2-4 depend from claim 1. These claims add features to claim 1 and include its method of building molecules that use free energy estimates that may be higher than a lowest free energy estimate possible for the molecule. Therefore, these claims are not rendered obvious by the DeLisi in view of *In re Gulack* for the same reason as claim 1 is not obvious. Applicants respectfully request that the obviousness rejection be withdrawn as it has been applied to claims 2-4 based on DeLisi in view of *In re Gulack*.

The Examiner has also rejected claims 1-4 for obviousness based on the combination of DeLisi in view of Hatada. The Examiner cited Hatada for allegedly teaching that three-dimensional structures of SH2 domain protein have been determined by X-ray crystallography. In the section of this Reply directed to overcoming the anticipation rejection and the previous portion of this section on obviousness, Applicants have demonstrated that DeLisi does not teach, suggest, or in any contemplate the feature of the present invention that is to use free energy estimates that may be higher than a lowest free energy estimate possible for the molecule. The Hatada reference when added to DeLisi does not cure this infirmity. As such, DeLisi in view of Hatada does not render claims 1-4 obvious. Thus, Applicants respectfully request that this rejection be withdrawn.

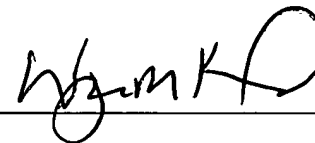
Conclusion

The present application is on final rejection. By this Reply, Applicants have traversed the Examiner's enablement rejection under 35 U.S.C § 112, anticipation rejection under 35 U.S.C. §102, and obviousness rejection under 35 U.S.C. § 103, thereby placing the present application in condition for allowance. The present application is new, non-obvious, and useful. Reconsideration and allowance of the claims are requested.

Respectfully submitted,

Dated:

4-07-04



Wayne M. Kennard
Registration No. 30,271
Attorney for Applicants

Hale and Dorr LLP
60 State Street
Boston, MA 02109
617-526-6183
617-526-5000 Fax